REMARKS

Claims 1, 2, 5-10, 23-25, 28 and 29 stand rejected. Claims 11-22, 26 and 27 were withdrawn, and were cancelled by amendment filed on November 21, 2001, but this amendment has not been entered, and entry of the amendment is respectfully requested.

Summary of the Invention The invention provides a novel human protein, referred to as P46, which is rapidly phosphorylated when cells are exposed to stress. P46 is localized in the endoplasmic reticulum. Applicants discovered that down-regulation of P46 using antisense oligonucleotides resulted in cytotoxicity and slowed cell growth. These results suggest that P46 carries out functions in the endoplasmic reticulum that are important for cell growth and viability. Importantly, Applicants also discovered significant down-regulation of the major P46 transcript in four out of four cases of brain tumors. This indicates that the activity of P46 may relate to tumor development and growth in the brain. The protein consists of 373 amino acids and the sequence is shown in SEQ ID NO:2. The protein was subsequently referred to as Nogo B following a literature report that did not, however, identify a function or activity for Nogo B (specification at page 8, lines 5-12).

Summary of prosecution history in parent application. Applicants respectfully submit that the Examiner erred when she rejected claims 1, 5-10, 23-25, 28 and 29 in the Advisory Action of June 11, 2002, because Applicants amended the claims to specifically address the remaining grounds of rejection in the Office Action dated September 21, 2001. To summarize, on February 26, 2001, the Examiner issued an Office Action (Paper No. 8) rejecting certain claims under 35 U.S.C. § 112, first and second paragraphs, under 35 U.S.C. § 102(e) over Bandman *et al.*, and under 35 U.S.C. § 103(a) over Bandman *et al.*, further in view of Milner *et al.* and James *et al.* On June 26, 2001, Applicants timely filed a response to address the various grounds of rejection, and amended claims 1, 2, 5 and 23. Claims 3 and 4 were cancelled.

In the Office Action mailed on September 21, 2001, the Examiner maintained the rejection of claims 1, 5-10, 23-25, 28 and 29 under 35 U.S.C. § 112, first paragraph, and the rejection of claims 23, 24, 28 and 29 under 35 U.S.C. § 103(a), for reasons of record. Claim 2 was newly rejected under 35 U.S.C. § 112, first paragraph, for indefiniteness. On November 21, 2001, Applicants timely filed a response canceling claims 11-22, 26, and 27 (which were drawn to non-elected subject matter) and amending claims 1, 2, 23, 28 and 29. Claims 23, 28 and 29

were amended to recite that the polynucleotide employed in the claimed method was not complementary to or identical to contiguous nucleotides between nucleotides 692 and 1385 of SEQ ID NO:1. As discussed at page 4, last full paragraph of the response, such language excluded binding to a sequence that was not specific to Nogo B polynucleotides, thus eliminating the grounds for rejection under 35 U.S.C. § 103(a).

On February 7, 2002, the Examiner issued an Advisory Action and indicated that the reply filed (i.e., received) on January 14, 2002, did not place the application in condition for allowance. The reasons provided were as follows:

1. The disclosure allegedly did not enable claims to "ex vivo" methods. As the ex vivo language is found in claims 23, 28 and 29 only, the rejection was not relevant to claims 1, 2 and 5-10.

2. The Examiner stated that delineation of nucleotides of SEQ ID NO:1 that aligned with corresponding amino acids of SEQ ID NO:2 would simplify the search related to the proposed amendments.

Applicants filed an Amendment of May 17, 2002. It is Applicants' position that the amendment filed on May 17, 2002, fully addressed both of the issues raised in the Advisory Action dated February 7, 2002, namely (a) deletion of the "ex vivo" claim language, and (b) indication of the polynucleotide and amino acid position correspondence, as requested by the Examiner for claim 1. [A copy of the polynucleotide/amino acid correspondence table is attached as Exhibit 1.] (During a telephone conference on March 29, 2002, the Examiner confirmed that this information was requested for claim 1.) In an Advisory Action dated June 11, 2002, the Examiner stated that this amendment had not been entered.

Applicants submit that the amendment filed on May 17, 2002 should have been entered. Applicants also respectfully submit that the Examiner erred in declining to enter the amendment filed on May 17, 2002, wherein the claim language objected to had already been submitted at an earlier stage during prosecution. In the Advisory Action dated February 7, 2002, the Examiner did not raise any issues regarding support in the specification for the amendments to claims 23, 28 and 29.

Thus, on two occasions (February 7, 2002 Advisory Action and March 29, 2002 telephone conference), the Examiner did not raise any objections to the amendment of claims 23, 28 and 29 as filed on November 21, 2001. The language of claims 23, 28 and 29 was first raised in the Advisory Action dated June 11, 2002. The Examiner did not enter the Amendment filed on May 17, 2002, stating as a reason that the "exclusion of nucleotide sequences 692-1385 of SEQ ID NO:1" in that amendment constituted new matter. Applicants submit that had the Examiner raised that issue upon first presentation of the Amendment as filed on November 21, 2001, Applicants could have addressed the Examiner's concern concurrent with addressing the issues raised in the February 7, 2002 Advisory Action.

Status of claims. On October 24, 2002, the Examiner issued a proposed Examiner's amendment, by facsimile, and sought Applicants' approval to amend the claims as follows:

(a) In claim 5, line 2, replace "at least one" with --a--.

(b) In claim 5, line 13, replace the period "." with a semicolon --;--.

(c) Cancel claims 23-25, 28 and 29.

Applicants discussed these amendments with the Examiner and respectfully declined to have them entered. Applicants also requested that the Examiner provide support for the position that 80% identity, as recited in claim 1, did not meet the Written Description Guidelines. The Examiner cited the Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001. Applicants reviewed this section in detail but did not find written support for the proposition that 95% identity does meet the Written Description Guidelines whereas 80% identity does not. On further telephone discussion, the Examiner agreed, and indicated that, nevertheless, it was Patent Office policy to make this distinction.

Applicants respectfully request that the Examiner provide an Affidavit in support of this position. (In re Sun, 31 USPQ2d, 1451, 1455 (Fed. Cir., 1993), stating that "the procedures established by 37 C.F.R. § 1.107(b) [now § 1.104(d)] expressly entitle an applicant, on mere request, to an examiner affidavit that provides such citations.") Applicants have identified a novel human polynucleotide sequence that encodes a full-length protein. It is Applicants' position that they are entitled to claim a nucleic acid comprising a polynucleotide at least 80% identical to the polynucleotides recited in claim 1; furthermore, the Examiner has not identified prior art that would preclude this claim scope. Applicants submit that there appear to

be no legal grounds for the Examiner's assertion that one of skill could identify all polynucleotides that have 95% identity, but not all polynucleotides with 80% identity. This is an arbitrary distinction, in view of the computer programs and analytical tools available to and used by one of skill in the art in this field. Therefore, the present claims retain the 80% identity language.

The proposed Examiner's amendment of October 24, 2002 is discussed below with reference to the individual amendments.

(a) Amendment of claim 5, line 2, to replace "at least one" with --a--. Claim 5, line 2, recites "...except for at least one conservative amino acid substitution..." This language is supported in the specification as filed at page 14, lines 1-3. In order to advance the prosecution, without acquiescing to the position of the U.S. Patent and Trademark Office as indicated in the Examiner's proposed amendment, Applicants have amended claim 5 to recite "- -between one and 50 conservative amino acid substitution- -" as supported in the specification at page 14, lines 3-6. Applicants have also added claims 30-37, which recite specific embodiments of the number of conservative amino acid substitutions, also as supported at page 14, lines 3-6. Applicants submit that claims 5 and 30-37 are fully supported by the specification as filed.

(b) Amendment of claim 5, line 13, replace the period "." with a semicolon --;--. Applicants agree with this amendment to correct a grammatical error, and claim 5 has been amended herein accordingly. Claim 5 is also amended to recite biological function of the polypeptide, and is supported in the specification at page 34, line 5 to page 35, line 29 and page 19, line 18 to page 20, line 5.

(c) Cancellation of claims 23-25, 28 and 29. Claims 23-25, 28 and 29 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bandman *et al.* (U.S. Patent No. 5,858,708) and further in view of Milner *et al.* and James. Bandman does not teach the polynucleotide sequence disclosed in the present application, corresponding to Nogo B. Instead, Bandman only discloses a sequence that is similar to the C-terminal end of the encoded Nogo B protein, from about amino acid 186 to the end of the molecule. Nogo B and the sequences taught in Bandman appear to be, at most, distinct forms of a larger family of proteins. The Examiner concurs with this evaluation, as the previous rejection of claims 1-10 was withdrawn in view of

the amendment to these claims to remove the reference to polynucleotides encoding certain shorter regions of the amino acid sequence corresponding to Nogo B.

Applicants previously sought to amend claims 23, 28 and 29 to recite that the methods did not employ a polynucleotide that was complementary to the region of Nogo B polynucleotide that overlaps with the Bandman sequence. Specifically, the claims as amended recited that the polynucleotide was not complementary or identical to contiguous nucleotides between nucleotide 692 and 1385 of SEQ ID NO:1. During a personal interview with the undersigned representative the PTO on October 17, 2002, the Examiner stated that this amendment did not find written support in the specification as filed, but that another amendment to accomplish this distinction from Bandman would be considered.

It is Applicants' continued position that claims 23, 28 and 29 are supported in the specification, because the specification provides for binding of an antisense oligonucleotide or a ribozyme in a manner that depends on the specific sequence of the Nogo B polynucleotide. At page 20, lines 16-20, the specification discloses specific reduction of Nogo B protein levels, and lines 20-23 disclose the "sequence-specific manner" of the binding.

However, to further the prosecution, Applicants have amended claims 23, 28 and 29 to recite that the antisense molecule or ribozyme comprises a sequence that is unique to Nogo B cDNA, as supported in the specification at least at page 22, lines 7-8, and at page 23, lines 2-5 and 19-21. Applicants submit that this amendment is consistent with the suggestion kindly made by the Examiner on October 17, 2002.

In view of the remarks and amendments herein, Applicants respectfully submit that claims 1, 2, 5-10, 23, 25, 28 and 29 are not subject to any of the grounds of rejection of record, and respectfully request that these claims and new claims 30-37 be allowed.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,
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